Citation:

Lim SS, Noakes M, Keogh JB, Clifton PM. Long-term effects of a low carbohydrate, low fat or high unsaturated fat diet compared to a no-intervention control. *Nutr Metab Cardiovasc Dis*. 2009 Aug 17.

PubMed ID: 19692216

Study Design:

Randomized Controlled Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To compare the long-term effects of three energy reduced, isocaloric diets, including very low carbohydrate, very low fat and high unsaturated fat diets, on weight loss and cardiovascular risk factors through a 15 month randomized control trial in overweight or obese individuals with elevated cardiovascular risks. The secondary purpose was to determine if the diets would result in significantly different effects compared to a no-intervention control after fifteen months.

Inclusion Criteria:

- 20 to 65 years of age
- BMI 28 kg/m^2 to 40 kg/m^2
- At least one cardiovascular disease risk factor other than obesity
- Informed written consent.

Exclusion Criteria:

- Under 20 or over 65 years of age
- BMI <28 kg/m^2 or >40 kg/m^2
- Use of hypoglycemic medication or drugs that affect insulin sensitivity
- History of heavy alcohol consumption
- History of metabolic disease
- History of coronary heart disease
- History of type one or type two diabetes
- Widely fluctuating exercise patterns
- Frequent dining out (more than twice per week and unable to cease).

Description of Study Protocol:

Recruitment: Through public advertisement

Design: Randomized controlled trial

Blinding used (if applicable): implied with measurements

Intervention:

- After being matched for age, gender, weight, and menopausal status, subjects were randomized to either the very low carbohydrate (VLC), very low fat (VLF), high unsaturated fat (HUF) or control group
- Diets
    - Same energy content, 6500 kilojoules
    - VLC diet contained 35% of energy as protein, 60% fat, 20% saturated fat and 4% carbohydrate
    - VLF diet contained 20% energy as protein, 10% fat, 3% saturated fat and 70% carbohydrate
    - HUF diet contained 20% energy as protein, 30% fat, 6% saturated fat, 8% polyunsaturated fat and 50% carbohydrate
- First three months provided intensive support
    - Subjects were provided with prescriptive meal plans and foods contributing to 65% energy of the meal plans
    - Individual dietary counseling every two weeks from a dietitian to monitor diet compliance
- Remaining 12 months
    - Subjects advised to maintain their allocated energy-restricted diet
    - Subjects in diet groups attended CSIRO outpatient clinic at six, nine, 12, and 15 months for measurements and individual visits by the dietitian for dietary advice
- Control group received no dietary intervention for the duration of the study

Statistical Analysis:

- Baseline differences between treatment groups were analyzed using one-way ANOVA
- Attrition rate assessed using Chi-squared analysis
- Nutrient intakes at 15 months assessed using one-way ANOVA with diet as fixed factor
- Pearson's correlation used to assess relationship between weight change and reported dietary intake
- Linear mixed effects model used to assess treatment outcomes, including partial data contributed by non-completers
- Group differences on change determined by post-hoc tests when a significant group-by-time interaction was present
- Changes in diet groups were combined and compared with changes in the control group using ANCOVA with baseline variables as covariates
- Regarding differences in weight and metabolic changes between diet groups, power analysis shows study with 60% power at a significance level of 0.05 to determine 1.0 kg difference in weight change between the diet groups
- Pertaining to differences between diet groups and control group, 76% power to determine 4.7 kg difference in weight changes between the intervention diets and control.

Data Collection Summary:

Timing of Measurements:

- Height measured at baseline
- Body weight measured at baseline, three, six, nine, 12 and 15 months for intervention groups and at baseline and 15 months for the control group
- Blood pressure measured at baseline, three and 15 months
- Fasting venous blood samples collected at baseline, three and 15 months for intervention groups and at baseline and 15 months for control group to evaluate plasma glucose, insulin and serum lipid concentrations
- Three day weighed food record (2 weekdays and 1 weekend day) at three, six, nine, 12 and 15 months for intervention groups and at baseline and 15 months for control group

Dependent Variables

- Weight change
- Fat mass
- Fasting insulin and glucose
- Fasting serum lipid concentrations
- Cardiovascular risk factors
- Blood pressure
- Level of adherence with prescribed diet

Independent Variables

- Prescribed isocaloric diet
- Dietary intake as with three day weighed food recorded reviewed and analyzed by dietitian using Diet/1 Nutrition Calculation

Control Variables

- Gender
- Age

Description of Actual Data Sample:

Initial N: 113 (48 males, 93 females)

Attrition (final N):

- 104 (17 males, 87 females) commenced the study
- 69 subjects (13 male, 56 female) completed the 15 month study
- Attrition rate:
    - VLC group: 43%
    - VLF group: 40%
    - HUF group: 50%
    - Control group: 17%

Age:

- No significant difference among groups, P=0.190
- VLC group: 48.3±7.6 years

- VLF group: 48.6±11.3 years
- HUF group: 47.2±10.5 years
- Control group: 43.1±10.7 years

Ethnicity: Not described

Other relevant demographics:

Anthropometrics

- Subjects were matched for age, gender, weight, and menopausal status
- Control group had significantly lower baseline total cholesterol, apolipoprotein B48, systolic blood pressure and diastolic blood pressure than treatment groups, P<0.05
- LDL cholesterol was significantly lower at baseline for non-completers (1.8±2.0 mmol/L) compared to study completers (3.4±1.1 mmol/L), P<0.001

Location: Australia

Summary of Results:

Key Findings:

- At three months, reported dietary intakes were consistent with the prescribed macronutrients profile of each diet
- At 15 months, intakes of fat, cholesterol, and monounsaturated fat remained significantly higher while carbohydrate intake was significantly lower in the VLC group compared to the VLF group
- Saturated fat intake was significantly higher in the VLC group compared to the HUF group at 15 months (P=0.024)
- All groups combined, total energy intakes were inversely correlated with protein intake (r= -0.55, P<0.001)
- Participants gained weight between three and 15 months
- All diet groups combined and compared against control group had significantly greater weight loss after correcting for baseline values (P=0.012)
- All groups combined weight loss at 15 months significantly correlated to higher protein intake (r=-0.38, P=0.009), lower fat intake (r= -0.31, P=0.037) and higher fiber intake (r= -0.30, P=0.038)
- At three months, total and LDL cholesterol increased in the VLC group but decreased in other diet groups (P=0.015) and differences between the diet groups were no longer significant at 15 months although diet groups had significantly greater decrease in total and LDL cholesterol compared to control group but the differences were no longer significant after correcting for baseline values (P>0.05)
- At three months, a significant time-by-group interaction was observed in HDL cholesterol, with an increase in the VLC group and a decrease in other diet groups (P=0.025) but differences were no longer observed at 15 months
- At three months, a significant time-by-group interaction was observed in triglycerides with a greater decrease in the VLC group compared to other diet groups (P=0.001) but differences were no longer observed at 15 months
- At three months, a significant time-by-group interaction was observed in homocysteine with an increase in the VLC group and a decrease in other diet groups (P=0.025) but no differences were observed at 15 months

- No significant time-by-group interactions were observed in C-reactive protein, folate, and apolipoprotein B at three or 15 months
- Significant time-by-group interactions were observed in fasting insulin between diet groups at three months but not at 15 months
- Systolic and diastolic blood pressure decreased in all diet groups at three months and at fifteen months when compared to control group, significant time-by-group interactions were observed ($P<0.05$)

Variables		VLC diet	VLF diet	HUF diet	Control	Statistical significance between groups
Weight, kg	3 month	-8.0±2.8	-6.7±3.5	-6.3±2.9	--	P=0.159
	15 month	-2.9±4.9	-2.1±4.7	-3.9±6.3	0.8±5.0	P=0.065
Total cholesterol, mmol/L	3 month	0.1±1.1	-0.5±0.8	-0.5±0.6	--	P=0.085
	15 month	-0.4±0.8	-0.3±0.8	-0.3±1.2	0.5±0.8	P=0.042
HDL cholesterol, mmol/L	3 month	0.1±0.2	-0.1±0.2	-0.1±0.2	--	P=0.025
	15 month	0.1±0.3	0.1±0.3	-0.1±0.2	0.1±0.2	P=0.979
LDL cholesterol, mmol/L	3 month	0.3±1.0	-0.4±0.6	-0.6±1.1	--	P=0.015
	15 month	-0.3±0.7	-0.3±0.7	-0.1±1.1	0.4±0.7	P=0.022
Triglyceride, mmol/L	3 month	-0.7±0.6	-0.1±0.6	-0.2±0.5	--	P=0.001
	15 month	-0.2±0.7	0.1±0.9	-0.3±0.8	-0.1±0.3	P=0.852
Cholesterol:HDL	3 month	-0.2±0.2	-0.2±0.1	-0.2±0.2	--	P=0.982
	15 month	-0.2±0.2	-0.3±0.1	-0.02±0.4	0.2±0.1	P=0.380
Triglyceride:HDL	3 month	-0.6±0.1	-0.03±0.1	-0.04±0.1	--	P=0.000
	15 month	-0.09±0.2	-0.05±1.8	-0.1±0.2	-0.1±0.1	P=0.917
Apolipoprotein B48, g/L	3 month	-0.1±0.3	-0.1±0.2	-0.1±0.1	--	P=0.410
	15 month	0.1±0.3	-0.1±0.2	-0.1±0.3	0.1±0.2	P=0.390
C-reactive protein, mg/L	3 month	1.2±12.2	0.3±5.0	-0.5±3.2	--	P=0.714
	15 month	-1.7±6.7	-2.1±2.5	-1.8±3.1	-1.4±3.2	P=0.144

Folate, nmol/L	3 month	-0.7±4.2	3.6±6.2	0.9±8.4	--	P=0.70
	15 month	-1.3±8.9	0.1±9.2	-6.0±8.7	-2.2±8.9	P=0.135
Homocysteine, µmol/L	3 month	0.6±1.4	-0.5±1.5	0.1±1.1	--	P=0.025
	15 month	0.4±1.2	-0.6±1.1	0.1±1.2	0.2±1.3	P=0.90
Vitamin B12, pmol/L	3 month	6.8+61.4	-4.6±49.1	-4.1±78.7	--	P=0.541
	15 month	33.5+76.9	18.9±66.9	41.9±73	27.2±71.5	P=0.880
Fasting insulin, mU/L	3 month	-3.9±3.7	3.0±13.8	-1.8±2.7	--	P=0.003
	15 month	-1.5±4.4	0.5±5.5	-1.7±4.0	-0.3±3.2	P=0.587
Fasting glucose, mmol/L	3 month	-0.1±0.3	0.1±0.6	-0.2±0.4	--	P=0.188
	15 month	0.1±0.3	0.3±0.6	-0.4±1.0	-0.1±0.6	P=0.215
Systolic blood pressure, mmHg	3 month	-10.5±12.7	-7.1±12.6	-3.1±14.5	--	P=0.172
	15 month	-10.6±10.6	-6.0±13.3	-5.4±13.3	1.9±8.3	P=0.011
Diastolic blood pressure, mmHg	3 month	-3.8±9.5	-2.1±11	-2.0±9.3	--	P=0.790
	15 month	-6.6±12.1	-7.5±8.7	-9.0±9.3	2.9±8.2	P=0.002

Other Findings:

- No gender differences were observed in any outcome.

Author Conclusion:

In conclusion, significant weight and diastolic blood pressure reduction were observed equally with VLC, VLF and HUF diets at 1 year after a 3-month intensive intervention, compared to an exacerbation of cardiovascular risk factors in the control group. These findings suggest that modest levels of adherence to any of these dietary patterns with minimal support would result in a greater benefit than no dietary intervention in individuals with increased cardiovascular risk.

Reviewer Comments:

- *Significant baseline differences between groups in terms of total cholesterol, apolipoprotein B48, systolic and diastolic blood pressure*
- *Lifestyle characteristics not assessed, including level of physical activity*
- *3 day weighed food records used to assess dietary intake which may introduce inaccuracies*
- *Power levels less than 80%.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	No
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	No
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	No
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes

3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A

6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	Yes
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	No
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	???
8.6.	Was clinical significance as well as statistical significance reported?	Yes

8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes